



INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference WBH	FOR FURTHER ACTION See Form PCT/IPEA/416	
International application No. PCT/EP2004/010733	International filing date (day/month/year) 15.09.2004	Priority date (day/month/year) 15.09.2003
International Patent Classification (IPC) or national classification and IPC G01F1/708, G01F1/56, G01F1/64, B01L3/00		
Applicant DIAGNOSWISS S.A. et al.		
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 8 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input checked="" type="checkbox"/> sent to the applicant and to the International Bureau) a total of 7 sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>		
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the opinion</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input checked="" type="checkbox"/> Box No. VII Certain defects in the International application</p> <p><input checked="" type="checkbox"/> Box No. VIII Certain observations on the international application</p>		
Date of submission of the demand 12.07.2005	Date of completion of this report 08.09.2005	
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Politsch, E Telephone No. +49 89 2399-8455 	

**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/EP2004/010733

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-22 as originally filed

Claims, Numbers

1-41 as originally filed

Drawings, Sheets

1/10-10/10 as originally filed

- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages
- ☐ the claims, Nos.
- ☐ the drawings, sheets/figs
- ☐ the sequence listing (*specify*):
- ☐ any table(s) related to sequence listing (*specify*):

4. ☒ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

- ☐ the description, pages
- ☒ the claims, Nos. 1-44
- ☐ the drawings, sheets/figs
- ☐ the sequence listing (*specify*):
- ☐ any table(s) related to sequence listing (*specify*):

* If item 4 applies, some or all of these sheets may be marked "superseded."

**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/EP2004/010733

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	3, 4, 26-28, 32-34, 36-38, 41
	No: Claims	1, 2, 5-25, 29-31, 35, 39, 40
Inventive step (IS)	Yes: Claims	
	No: Claims	3, 4, 26-28, 32-34, 36-38, 41
Industrial applicability (IA)	Yes: Claims	1-41
	No: Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

1. CITED DOCUMENTS

The following documents cited in the International Search Report are referred to:

- D1: WO 03/004160 A (DIAGNOSWISS SA; ROSSIER, JOEL, S; MICHEL, PHILIPPE; REYMOND, FREDERIC) 16 January 2003 (2003-01-16)
- D2: WU J ET AL: "Electrochemical time of flight flow sensor" SENSORS AND ACTUATORS A, ELSEVIER SEQUOIA S.A., LAUSANNE, CH, vol. 97-98, 1 April 2002 (2002-04-01), pages 68-74, XP004361584 ISSN: 0924-4247
- D3: US 2002/179445 A1 (ALAJOKI MARJA LIISA ET AL) 5 December 2002 (2002-12-05)
- D4: US-A-5 992 820 (FARE ET AL) 30 November 1999 (1999-11-30)

2. REMARKS ON I. BASIS OF THE REPORT

The amendments filed with the letter dated 12 July 2005 introduce subject-matter which extends beyond the content of the application as filed, contrary to Article 34(2)(b) PCT.

2.1 Claim 1

(a) New claim 1 defines that the "integrated electrode is adapted to monitor the solution flow at the precise location of said integrated electrode by amperometric measurement". Original claim 17, which should seemingly serve as a basis for the amendment, defines that the "integrated electrode has a precise size and location in said microfluidic system". The former formulation cannot be deduced from the latter and infringes Article 34(2)(b) PCT therefore.

(b) The last passage of new claim 1 reads "wherein said integrated electrode is in addition adapted to electrochemically detect an analyte of interest during an assay".

Said adaptation, however, cannot unambiguously be derived from the application as originally filed: no instance teaching the (specific) adaptation of the electrode for electrochemically detecting an analyte (additionally to the detection for flow measurement purposes) can be found in the originally filed documents.

2.2 Claims 2, 19, 27

See 2.1 (a).

2.3 Claims 17, 37, 38

See 2.1 (b).

2.4 Claims 29, 39

It cannot unambiguously be derived from the application as originally filed that "the solution flow is continuously monitored ..., except during the electrochemical detection of said analyte".

2.5 Claims 41-44

The subject-matter introduced by new claims 41 (and claim 42, which depends on claim 41), 43 and 44 is not supported by the original application.

2.6 Due to the substantial infringements of Article 34(2)(b) PCT the examination as to novelty and inventive step has been carried out on the originally filed claim set.

**3. REMARKS ON V. REASONED STATEMENT WITH REGARD TO NOVELTY,
INVENTIVE STEP OR INDUSTRIAL APPLICABILITY**

Articles 33(2), (3) PCT

The subject-matter of claims 1, 2, 5-25, 29-31, 35, 39, 40 is not new in the sense of Article 33(2) PCT.

The subject-matter of claims 3, 4, 26-28, 32-34, 36-38, 41 appears to lack an inventive step in the sense of Article 33(3) PCT.

3.1 Claims 1 and 30

Document D1 discloses (see e.g. Figs. 1A or 1B)
an electrochemical flow monitoring device, comprising
a microfluidic system comprising at least one covered (p. 4, l. 1-3) microchannel having an inlet and an outlet (see e.g. Figs. 1A or 1B);
means for applying a pressure difference between the inlet and the outlet of said microfluidic system such as to generate a flow of solution within said covered microchannel (see e.g. p. 13, l. 23-27);
wherein the microfluidic system has at least one electrode (5) for monitoring said flow of

solution by measuring an electrochemical property of said solution (see e.g. p. 4, l. 24 - p. 5, l. 3).

Therefore, the subject-matter of claim 1 (and the corresponding method claim 30) is not new.

3.2 Claim 2

See p. 4, l. 24 - p. 5, l. 4 of D1: the 'electroactive species' is obviously a kind of 'reporter molecule'.

3.3 Claims 3-7, 32-34

The different alternatives for inducing a pressure difference are obvious; the selections defined in claims 5-7 are explicitly mentioned in D1.

3.4 Claim 8

See, e.g., the paragraph starting with line 16 on p. 4 of D1.

3.5 Claims 9, 10

See e.g. claims 1 and 6 of D1.

3.6 Claims 11, 13

See e.g. claim 10 of D1.

3.7 Claim 12

See e.g. claims 16 and 17 or p. 12, second paragraph of D1.

3.8 Claim 14

See claim 12 of D1.

3.9 Claim 15

See the electrodes (5) of D1.

3.10 Claim 16

See p. 12, l. 12-14 and p. 21, l. 5-7 of D1.

3.11 Claims 17, 18

See D1.

3.12 Claim 19

See claim 17 of D1.

3.13 Claim 20

See e.g. p. 20, l. 28-29 of D1.

3.14 Claim 21

See e.g. claim 6 or p. 8, second paragraph - p. 9, first paragraph of D1.

3.15 Claims 22-24

See e.g. claims 23 and 24 of D1.

3.16 Claim 25, 35

See e.g. claim 38 of D1.

3.17 Claims 26, 27, 36, 37

These claims describe obvious possibilities to stop material flow through the microchannel(s) and cannot be regarded as involving an inventive step.

3.18 Claim 28, 38

See col. 1 and col. 2, section 'Summary of the Invention', of document D4. It is clear to the skilled person that the electrochemical bubble generation disclosed in D4 can be used in a microfluidic flow monitoring device according to D1.

3.19 Claim 29

Such affinity assays and incubation are also mentioned in D1 (p. 15, l. 20-24 and p. 18, second paragraph).

3.20 Claim 31

See Fig. 8 and the related passages of the description of D1.

3.21 Claims 39, 40

See Fig. 10 and the related passages of the description of D1.

3.22 Claim 41

Optical sensors are widely used in microfluidic detection systems, see e.g. D3. To use such sensors in an apparatus or method as disclosed in D1 does certainly not require any inventive skill.

4. REMARKS ON VII. CERTAIN DEFECTS IN THE INTERNATIONAL APPLICATION

4.1 Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents D1-D4 is not mentioned in the description, nor are these documents identified therein.

4.2 The features of the claims are not provided with reference signs placed in parentheses (Rule 6.2(b) PCT).

5. REMARKS ON VIII. CERTAIN OBSERVATIONS ON THE INTERNATIONAL APPLICATION

Lack of clarity (Article 6 PCT)

Some claims relating to the flow monitoring device (but not to the use of this device, as it appears to be appropriate) define features concerning the use of the device: e.g., claim 21 defines that 'one electrode serves to electrochemically detect an analyte...'. This definition does obviously not relate to the device per se and does therefore make no contribution to the claims which claim 21 refers to.

Hence, the additional subject-matter of this claims is unclear.